Remarks

The Applicants acknowledge the withdrawal from consideration of Claims 29-31, and 33. Accordingly, the Applicants have cancelled these claims and reserve the right to file one or more divisional applications based on the subject matter of these claims. The Office Action states that Claims 1-28 have been cancelled. The Applicants respectfully submit that the Applicants' response to the Restriction Requirement filed September 4, 2003, merely elected without traverse Group II, including Claim 32. Consequently, the Applicants did not cancel Claims 1-28. Nevertheless, the Applicants hereby cancel Claims 1-28 and reserve the right to file one or more divisional applications directed to the subject matter of these claims. Consequently, Claim 32 is currently under examination.

In accordance with the Examiner's helpful suggestion, the Applicants have amended the Specification to attend to minor informalities. Further, in accordance with Examiner's helpful suggestions, the Applicants have amended Claim 32 to place it into independent form. The Applicants have also amended Claim 32 to recite a transgenic mouse to obviate the rejection under 35 U.S.C §101. In light of this amendment, the Applicants have also amended Claim 32 to refer to SEQ ID NO: 5, which corresponds to murine TASK. Support for this amendment can be found in Fig. 8 of the Specification and the Sequence listing submitted with the Application. Finally, the Applicants have amended Claim 32 to delete the term "represented," and insert the term "comprising." No new matter has been added.

Claim Rejection Under 35 U.S.C. §112, First Paragraph

Claim 32 has been rejected under 35 U.S.C. §112, first paragraph. The Applicants respectfully submit that as a result of the amendment the rejection of Claim 32 is obviated.

The Applicants respectfully submit that the transgenic non-human animals of Claim 32 do not have to generate a phenotype to determine if the knock-out of SEQ ID NO: 5 was successful. Specifically, one skilled in the art would readily recognize the use of the "marker gene" strategy to signal proper homologous recombination in a non-human cell. In this well-known strategy, the introduced gene construct has its sequence disrupted by an inserted antibiotic-resistant gene, such as by a gene coding for neomycin resistance. If the construct undergoes homologous recombination with the endogenous copy of the gene, the endogenous gene is disrupted but the antibiotic-resistance gene remains functional, allowing cells that incorporated the gene to be selected in a culture for resistance to the neomycin drug G418. The use of marker genes has been employed in homologous recombination for over a decade.

However, antibiotic resistance on its own shows only that the cells have taken up and integrated the neomycin-resistance gene. To be able to select for those cells in which homologous recombination has occurred, the ends of the construct usually carry the thymidine kinase gene from the herpes simplex virus (HSV-tk). Cells that incorporate DNA randomly usually retain the entire DNA construct including HSV-tk, whereas homologous recombination between the construct and cellular DNA, the desired result, involves the exchange of homologous DNA sequences so that the nonhomologous HSV-tk genes at the ends of the construct are eliminated. Cells carrying HSV-tk are killed by the antiviral drug ganciclovir, and so cells with homologous recombination have the unique feature of being resistant to both neomycin and ganciclovir, allowing them to be selected efficiently when these drugs are added to the cultures.

Moreover, the Applicants respectfully submit that a reading of Leonard (1995, Immunological Reviews, Vol. 148 pgs. 98-113) merely indicates that γ_c gene is involved in a number

of molecular functions. One skilled in the art would readily understand that one gene can be involved in multiple cellular functions and, as a result, the knock-out of that gene exhibits a number of different effects on cellular processes. This is termed pleiotropy. Pleiotropy is where a single gene has more than one phenotypic expression. In fact, pg. 108 of Leonard states that "one also needs to consider the principles of 'cytokine receptor subunit pleiotropy.'" As a result, the Applicants respectfully submit that Leonard does not in anyway indicate that the "phenotype of transgenic animals was unpredictable." Rather, Leonard merely indicated that the γ_c gene was pleiotropic.

The Applicants respectfully submit that Griffiths (1998, Microscopy Research and Technique, Vol. 41, pgs. 344-358) teach a knock-out having *Plp* gene disrupted. Prior to the investigation, PLP was known as an abundant myelin protein. However, the function of PLP was unknown. The resulting knock-out mouse revealed did not exhibit the *jimpy* phenotype, but did exhibit axonal swellings, which are associated with defects in axonal transport. (See page 351-353). The Applicants respectfully submit that this is one of a number of examples where a knock-out is generated using an uncharacterized protein and the resulting phenotype is identified through known processes by people skilled in the art.

The Applicants respectfully submit that one skilled in the art could readily use the Applicants' Specification to create a "knock-out" mouse and subsequently test the phenotype. This is especially true in light of the Applicants' detailed disclosure describing the biophysical and regulation properties of TASK channels along with its regulation and tissue distribution. (See pages 18-23 of the Applicants' Specification). Thus, unlike Griffiths, the Applicants have fully described and characterized TASK proteins prior to the generation of a knock-out mouse. As a result, the

elucidation of the phenotype of a knock-out mouse deficient in TASK could readily be obtained by anyone skilled in the art.

In view of the foregoing, the Applicants respectfully submit that the aforementioned technique would readily allow one skilled in the art to produce knock-out mice , wherein the effects of knock-out-specific genes can be analyzed. Once recombination is confirmed, one skilled in the art can readily assay the absence of a particular gene's function. In this case, the nucleic acid sequence is SEQ ID NO: 5. In addition, the aforementioned technique allows identification of essential domains by determining whether a function can be restored by introducing different mutated copies of the gene back into the genome through transgenesis.

Claim Rejection Under 35 U.S.C. §102(b)

Claim 32 has been rejected under 35 U.S.C §102(b) as anticipated by Mullins. The Applicants respectfully submit that Mullins does not disclose a knock-out mouse deficient in the expression of SEQ ID NO: 5. As a result the rejection of Claim 32 is now moot. The Applicants respectfully request withdrawal of the rejection of Claim 32 as anticipated by Mullins.

In view of the foregoing, the Applicants respectfully submit that the application is now in a condition for allowance, which is respectfully requested.

Respectfully submitted,

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